

RECEIVED  
CENTRAL FAX CENTER

MAY 15 2007

## Amendments to the Claims:

1. (Currently Amended) A transgenic mouse comprising a somatic cell, comprising:

(a) in a first chromosome of a chromosome pair, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase; and

(b) at a homologous location of a second chromosome of the chromosome pair, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase, wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes;

wherein recombinase-promoted somatic mitotic recombination between the target sites yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first-second~~ second-first marker-specific signal, the second X-segregated progeny cell produces a ~~second-first~~ first-second marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

2. (Previously Amended) The mouse of claim 1, wherein the recombinase and target sites are selected from the group consisting of Cre/loxP and FLP/rt.
3. (Previously Amended) The mouse of claim 1, wherein the first and second markers are GFP and RFP.
4. (Previously Amended) The mouse of claim 2, wherein the recombinase and target sites are Cre/loxP, and the first and second markers are GFP and RFP.
5. (Previously Amended) The mouse of claim 1, wherein the first and second markers are transcriptional regulators.
6. (Previously Amended) The mouse of claim 1, wherein the somatic cell further comprises a genetic construct comprising a cell-type specific promoter operably linked to a sequence encoding the recombinase.
7. (Previously Amended) The mouse of claim 1, wherein the somatic cell further comprises a genetic construct comprising a drug-inducible promoter operably linked to a sequence encoding the recombinase, wherein the drug is selected from the group consisting of tamoxifen and doxycycline.
8. (Withdrawn - Currently Amended) A method of making a mouse according to claim 1, the method comprising the steps of:
  - (a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;
  - (b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first-second~~ marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

9. (Withdrawn - Currently Amended) A method of making a mouse according to claim 2, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably

linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first~~ first-second marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

10. (Withdrawn - Currently Amended) A method of making a mouse according to claim 3, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase, wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first~~ second marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

11. (Withdrawn - Currently Amended) A method of making a mouse according to claim 4, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding

an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first~~ second marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

12. (Withdrawn - Currently Amended) A method of making a mouse according to claim 5, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the first second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a first-second marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

13. (Withdrawn - Currently Amended) A method of making a mouse according to claim 6, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first~~ second marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the



first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

14. (Withdrawn - Currently Amended) A method of making a mouse according to claim 7, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic mitotic recombination between the target sites in a differentiated progeny cell yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the first second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the second first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first-second~~ marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

15. (Withdrawn - Original) The method of claim 8, wherein the pluripotent cell is an ES cell.

16. (Withdrawn - Original) The method of claim 8, wherein the pluripotent cell is an egg cell.

17. (Withdrawn - Previously Amended) A method of making a mouse according to claim 1, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

18. (Withdrawn - Previously Amended) A method of making a mouse according to claim 2, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

19. (Withdrawn - Previously Amended) A method of making a mouse according to claim 3, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

20. (Withdrawn - Previously Amended) A method of making a mouse according to claim 4, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

21. (Withdrawn - Previously Amended) A method of making a mouse according to claim 5, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

22. (Withdrawn - Previously Amended) A method of making a mouse according to claim 6, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably

linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

23. (Withdrawn - Previously Amended) A method of making a mouse according to claim 7, the method comprising the steps of:

(a) introducing in a first chromosome of a chromosome pair of a pluripotent cell, a polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of a recombinase;

(b) introducing at a homologous location of a second chromosome of the chromosome pair of the pluripotent cell, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes; and

(c) growing the cell to obtain a mouse comprising differentiated progeny cells of the pluripotent cell, wherein recombinase-promoted somatic recombination between the target sites in a differentiated progeny cell yields a recombined cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome

comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the recombined cell produces both a first and a second marker specific-signal.

24. (Withdrawn - Original) The method of claim 17, wherein the pluripotent cell is an ES cell.

25. (Withdrawn - Original) The method of claim 17, wherein the pluripotent cell is an egg cell.

26. (Currently Amended) A transgenic mouse comprising a somatic cell, comprising:

(a) in a first chromosome of a chromosome pair, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first fluorescent marker and a C-terminal portion of a second fluorescent marker separated by a first target site of a recombinase; and

(b) at a homologous location of a second chromosome of the chromosome pair, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase,

wherein presence of the recombinase in the cell promotes recombination between the target sites of the first and second chromosomes;

wherein recombinase-promoted somatic mitotic recombination between the target sites yields alternative pairs of X- or Z-segregated progeny cells,

wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker, and

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the

second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first-second~~ first marker-specific fluorescent signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific fluorescent signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific fluorescent signal, and the second Z-segregated progeny cell produces both a first and a second marker-specific fluorescent signal.

27. (Previously Presented) The mouse of claim 26, wherein the first and second markers are GFP and RFP.

28. (Previously Presented) The mouse of claim 26, wherein the recombinase and target sites are Cre/loxP, and the first and second markers are GFP and RFP.

29. (Currently Amended) A method to generate and mark chromosome recombination in somatic cells in a mouse, the method comprising:

crossing a first transgenic mouse that comprises a genome-incorporated, promoter-operably-linked site-specific recombinase-encoding transgene, with a second transgenic mouse that comprises in a first chromosome of a chromosome pair ~~(a)~~, a first polynucleotide comprising a first promoter operably linked to a first chimeric sequence encoding an N-terminal portion of a first marker and a C-terminal portion of a second marker separated by a first target site of the recombinase, and at a homologous location of a second chromosome of the chromosome pair ~~[[:]~~, a second polynucleotide comprising a second promoter operably linked to a second chimeric sequence encoding an N-terminal portion of the second marker and a C-terminal portion of the first marker separated by a second target site of the recombinase, to generate a progeny mouse that comprises the chromosome pair and expresses the recombinase,

wherein expression of the recombinase promotes recombination between the target sites of the first and second chromosomes in somatic cells of the progeny mouse,

wherein the recombinase-promoted somatic mitotic recombination between the target sites yields alternative pairs of X- or Z-segregated progeny cells,



wherein the X-segregated progeny cells comprise a first progeny cell comprising the first chromosome, and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~first~~ second marker; and a second progeny cell comprising the second chromosome, and a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the ~~second~~ first marker,

wherein the Z-segregated progeny cells comprise a first progeny cell comprising the first chromosome and the second chromosome, and a second progeny cell comprising a recombined variant of the first chromosome comprising the first promoter operably linked to a sequence encoding the N- and C-terminal portions of the first marker; and a recombined variant of the second chromosome comprising the second promoter operably linked to a sequence encoding the N- and C-terminal portions of the second marker,

wherein the first X-segregated progeny cell produces a ~~first-second~~ marker-specific signal, the second X-segregated progeny cell produces a ~~second~~ first marker-specific signal, the first Z-segregated progeny cell produces neither a first nor second marker-specific signal, and the second Z-segregated progeny cell produces both a first and a second marker specific-signal.

30. (Previously Presented) The method of claim 29, wherein the recombinase and target sites are Cre/loxP, and the first and second markers are GFP and RFP.